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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/145,180	09/01/1998	JIA-HE LI	23356-M5	5665

7590 05/24/2004

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/145,180	LI ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *184-233* is/are pending in the application.

4a) Of the above claim(s) *193,195,197-206,208,214,215 and 217-233* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *184-192,194,207,209-213 and 216* is/are rejected.

7)☒ Claim(s) *196* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' remarks submitted March 10, 2004 is acknowledged.

Initially, note Claims 184-233 are pending, claims 193, 195, 197-206, 208, 214, 215 and 217-233 are withdrawn as drawn to nonelected species (see paper mailed December 4, 2001).

The Claims have been examined insofar as they read on the searched species. The searched species are 6(5H)-phenanthrindinone, 2-nitro-6 (5H)-phenanthrindinone (recited in claim 194), and their homologs

Claim Objections

1. Claim 196 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims Rejections 35 U.S.C. - 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 184-192, 194, 207, 209-213 and 216 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weltin et al. (AT of page 5, IDS paper No. 3) in view of Banasik et al. (AH, IDS paper No. 4), and Endres et al. (AT of page 2, IDS paper No. 3)

3. Weltin et al. (AT of page 5, IDS paper No. 3) teach that 6(5H)-phenanthrindinone, an isoquinoline derivative, is a potent inhibitor of poly (ADP-ribose) polymerase (PARP). See the abstract and Figure 1.

Weltin et al. do not teach expressly the employment of a substituted 6(5H)-phenanthrindinone, 2-nitro-6 (5H)-phenanthrindinone, for treating ischemia.

However, Endres et. al. (AT of page 2, IDS paper No. 3) teach a method of treating ischemia by inhibition of PARP activity. See page 1144, third paragraph. Banasik et al teaches that 2-nitro substituted 6(5H)-phenanthrindinone have more inhibition activity against PARP than 6(5H)-phenanthrindinone. (IC_{50} 0.35 μM). See page 1573 right column, compound No. 3.

Therefore it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ substituted 6(5H)-phenanthrindinone, e.g., 2-nitro-6 (5H)-phenanthrindinone for treating ischemia because PARP inhibitors are known to be useful for treating ischemia, and 2-nitro-6 (5H)-phenanthrindinone is a more potent PARP inhibitor than 6(5H)-phenanthrindinone. Further, it would have been obvious to employ 2-nitro-10-methyl-6 (5H)-phenanthrindinone for treating ischemia since it is a homologous of 2-nitro-6 (5H)-phenanthrindinone, i.e., they differ only by a CH_2 group. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. In re Hass, 60 USPQ 544 (CCPA 1944); In re Henze, 85 USPQ 261 (CCPA 1950).

Response to the Arguments

Applicants' remarks submitted March 10, 2004 have been fully considered, but are not persuasive for reasons discussed below.

4. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The cited references, as a whole, teaches the usefulness of PARP inhibitors for treating ischemia, and 6(5H)-phenanthrindinone, and 2-nitro-6 (5H)-phenanthrindinone are PARP inhibitors. Therefore, it would have been obvious to employ such compounds or its homologs for treating ischemia. Applicants' attention is further directed to Banasik reference, which disclosed that among the known PARP inhibitors, 2-nitro-6 (5H)-phenanthrindinone is one of the few potent inhibitors.

5. Applicants further contend that the examiner uses a per se rule as to the homologs. The examiner did not use per se rule, but considered al aspects, including the teachings of the prior art. Prior art teaches 6(5H)-phenanthrindinone, and its substituted derivatives, e.g., 2-nitro-6 (5H)-phenanthrindinone, are known PARP inhibitors, it would have been reasonably expected their homologs are similarly useful.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (571)272-0632. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9302.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

SHENGJUN WANG
PRIMARY EXAMINER

Shengjun Wang

May 18, 2004